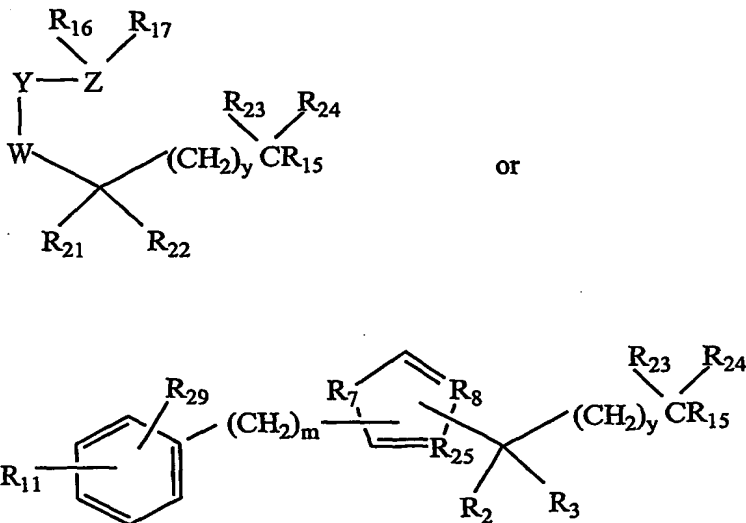


Claims:

1. A compound represented by the formula:



5

wherein

W is $\text{CR}_{27}\text{R}_{28}$ or $(\text{CH}_2)_n\text{NH}(\text{CO})$;

wherein R_{27} and R_{28} are independently selected from the group consisting of H, halo and hydroxy;

Y is selected from the group consisting of a bond, CR_9R_{10} , carbonyl, NH, O or

10 S;

wherein R_9 and R_{10} are independently selected from the group consisting of H, halo, hydroxy and amino;

Z is CH_2 , aryl, halo substituted aryl or heteroaryl;

R_{11} and R_{16} are independently selected from the group consisting of $\text{C}_5\text{-C}_{12}$

15 alkyl, $\text{C}_5\text{-C}_{12}$ alkenyl, $\text{C}_5\text{-C}_{12}$ alkynyl, $\text{C}_5\text{-C}_{12}$ alkoxy, $(\text{CH}_2)_p\text{O}(\text{CH}_2)_q$, $\text{C}_5\text{-C}_{10}$ (aryl) R_{20} , $\text{C}_5\text{-C}_{10}$ (heteroaryl) R_{20} , $\text{C}_5\text{-C}_{10}$ (cycloalkyl) R_{20} , $\text{C}_5\text{-C}_{10}$ alkoxy(aryl) R_{20} , $\text{C}_5\text{-C}_{10}$ alkoxy(heteroaryl) R_{20} and $\text{C}_5\text{-C}_{10}$ alkoxy(cycloalkyl) R_{20} ;

wherein R_{20} is H or $\text{C}_1\text{-C}_{10}$ alkyl;

R_{29} is H or halo;

20 R_{17} is selected from the group consisting of H, halo, NH_2 , $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, $\text{C}_1\text{-C}_6$ alkylamino, $\text{C}_1\text{-C}_6$ alkylcyano and $\text{C}_1\text{-C}_6$ alkylthio;

R_2 , and R_{21} are both NH_2 ;

R_3 is selected from the group consisting of H, C₁-C₆ alkyl, (C₁-C₄ alkyl)OH, and (C₁-C₄ alkyl)NH₂;

R_{22} is selected from the group consisting of C₁-C₆ alkyl, (C₁-C₄ alkyl)OH and (C₁-C₄ alkyl)NH₂;

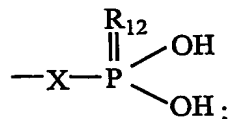
5 R_{23} is selected from the group consisting of H, F, CO₂H, OH, C₁-C₆ alkyl, (C₁-C₄ alkyl)OH, and (C₁-C₄ alkyl)NH₂;

R_{24} is selected from the group consisting of H, F and PO₃H₂, or R_{23} together with R_{24} and the carbon to which they are attached form a carbonyl group;

R_{25} , R_7 and R_8 are independently selected from the group consisting of O, S, 10 CHR₂₆, CHR₂₆, NR₂₆, and N;

wherein R_{26} is H, F or C₁-C₄ alkyl;

R_{15} is selected from the group consisting of hydroxy, phosphonate, and



wherein R_{12} is selected from the group consisting of O, NH and S;

15 X is selected from the group consisting of O, NH and S;

y and m are integers independently ranging from 0 to 4;

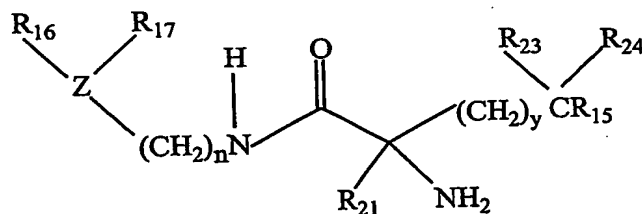
p and q are integers independently ranging from 1 to 10;

n is an integer ranging from 0 to 10;

or a pharmaceutically acceptable salt or tautomer thereof, with the proviso that W and

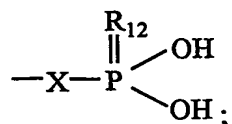
20 Y are not both methylene.

2. The compound of claim 1 wherein the compound is represented by the formula:



25 wherein

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and



wherein X and R₁₂ are independently selected from the group consisting of O and S;

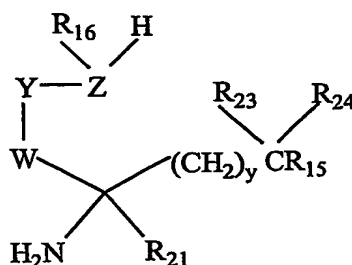
- 5 R₂₃ and R₂₄ are independently selected from the group consisting of H, F and C₁-C₄ alkyl;
or a pharmaceutically acceptable salt or tautomer thereof.

- 10 3. The compound of claim 2 wherein
y is 0 or 1;
n is 1-10;
Z is CH₂; and
R₁₇ is H.

- 15 4. The compound of claim 2 wherein
y is 0 or 1;
n is 0;
Z is C₅-C₆ aryl or C₅-C₆ heteroaryl;
R₁₆ is selected from the group consisting of C₅-C₁₂ alkyl C₂-C₁₂ alkenyl or C₅-
20 C₁₂ alkoxy; and
R₁₇ and R₂₃ are each H.

5. The compound of claim 4 wherein
Z is C₅-C₆ aryl;
25 R₂₄ is H; and
R₂₁ is selected from the group consisting of C₁-C₄ alkyl, and (C₁-C₄ alkyl)OH.

6. The compound of claim 1 wherein the compound is represented by the
formula:



wherein Z is aryl or heteroaryl;

R₁₆ is selected from the group consisting of C₅-C₁₂ alkyl, C₅-C₁₂ alkenyl, C₅-C₁₂ alkynyl and C₅-C₁₂ alkoxy;

Y is selected from the group consisting of CHOH, CF₂, CFH, carbonyl, NH, O and S;

W is CR₂₇R₂₈;

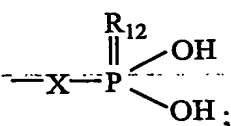
wherein R₂₇ and R₂₈ are independently selected from the group consisting of H, halo and hydroxy;

R₂₁ is selected from the group consisting of C₁-C₆ alkyl, (C₁-C₄ alkyl)OH and (C₁-C₄ alkyl)NH₂;

R₂₃ is selected from the group consisting of H, F, CO₂H, C₁-C₆ alkyl, (C₁-C₄ alkyl)OH, and (C₁-C₄ alkyl)NH₂;

R₂₄ is selected from the group consisting of H, F and PO₃H₂, or R₂₃ together with R₂₄ and the carbon to which they are attached form a carbonyl group;

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and



wherein X and R₁₂ are independently selected from the group consisting of O and S;

y is an integer ranging from 0 to 4;

or a pharmaceutically acceptable salt or tautomer thereof.

7. The compound of claim 6 wherein R₂₃ and R₂₄ are both H;

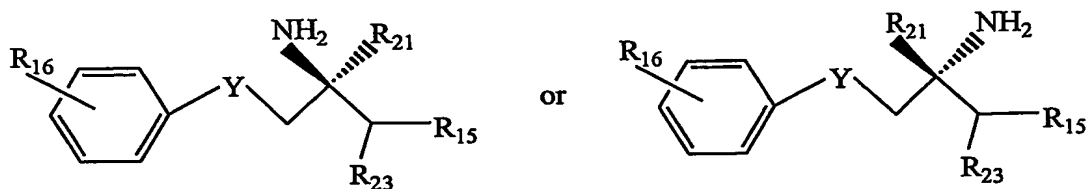
R_{27} and R_{28} are independently selected from the group consisting of H and F;

Z is C_5 - C_6 aryl or C_5 - C_6 heteroaryl;

R_{21} is selected from the group consisting of OH, C_1 - C_4 alkyl, and (C_1 - C_3 alkyl)OH; and

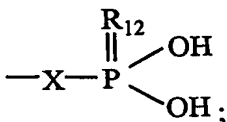
5 y is 0 or 1.

8. The compound of claim 6 wherein the compound is represented by the formula:



10

wherein R_{15} is selected from the group consisting of hydroxy, phosphonate,



and

wherein X and R_{12} are independently selected from the group consisting of O and S;

15 R_{21} is selected from the group consisting of C_1 - C_3 alkyl and (C_1 - C_4 alkyl)OH;

R_{23} is selected from the group consisting of H, F, C_1 - C_3 alkyl and (C_1 - C_4 alkyl)OH;

or a pharmaceutically acceptable salt thereof.

20

9. The compound of claim 8 wherein Y is selected from the group consisting of carbonyl, NH and O.

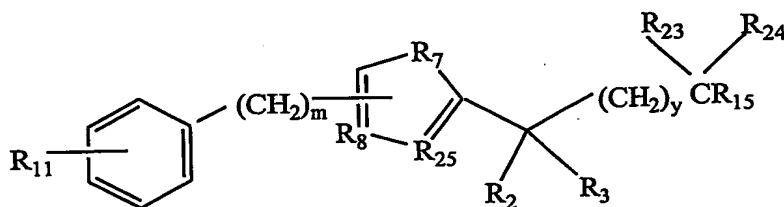
10. The compound of claim 9 wherein

R_{15} is OH; and

25

R_{23} is selected from the group consisting of H, F and C_1 - C_3 alkyl; or a pharmaceutically acceptable salt thereof.

11. The compound of claim 1 wherein the compound is represented by the formula:



wherein

5 R_{11} is selected from the group consisting of C₅-C₁₂ alkyl, C₅-C₁₂ alkenyl and C₅-C₁₂ alkynyl;

R_7 and R_8 are independently selected from the group consisting of O, S, CHR₂₆, CHR₂₆, NR₂₆, and N;

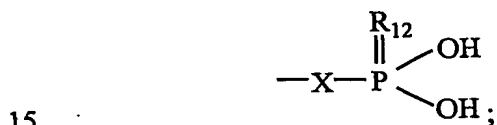
wherein R_{26} is H, F or C₁-C₄ alkyl;

10 R_{25} is N or CH;

R_2 is NH₂;

R_3 is selected from the group consisting of H, C₁-C₄ alkyl, (C₁-C₄ alkyl)OH, and (C₁-C₄ alkyl)NH₂;

R_{15} is selected from the group consisting of hydroxy, phosphonate, and



wherein X and R_{12} is selected from the group consisting of O and S;

R_{23} is selected from the group consisting of H, F, OH, C₁-C₄ alkyl, CO₂H and C₁-C₄ alkyl;

R_{24} is selected from the group consisting of H, F, C₁-C₄ alkyl and PO₃H₂, or

20 R_{23} together with R_{24} and the carbon to which they are attached form a carbonyl group; and

y and m are integers independently ranging from 0 to 4;

or a pharmaceutically acceptable salt or tautomer thereof.

25 12. The compound of claim 11 wherein m is 0;

y is 0 or 1;

R₂₅ is CH;

R₂₃ is H or F; and

R₂₄ is selected from the group consisting of H, F and C₁-C₄ alkyl.

5

13. The compound of claim 11 wherein R₃ is selected from the group consisting of C₁-C₃ alkyl and (C₁-C₄ alkyl)OH.

14. The compound of claim 12 or 13 wherein

10

R₇ is NH; and

X is O;

or a pharmaceutically acceptable salt or tautomer thereof.

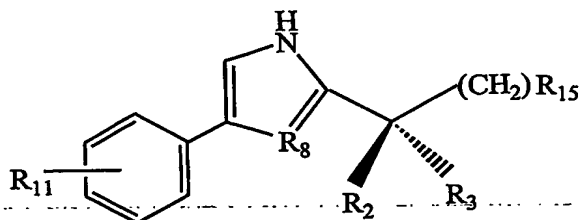
15. The compound of claim 14 wherein

15

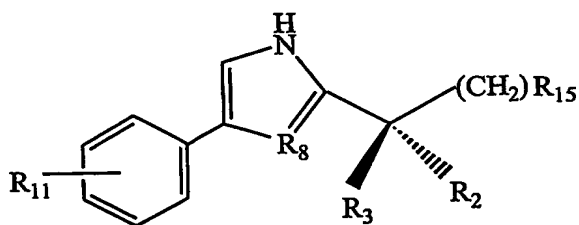
y is 0; and

R₁₅ is OH.

16. The compound of claim 13 wherein the compound is represented by the formula:



or



20

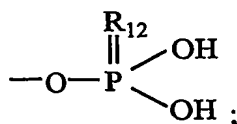
wherein R₁₁ is C₅-C₁₈ alkyl or C₅-C₁₈ alkenyl; and

R₈ is N;

or a pharmaceutically acceptable salt or tautomer thereof.

17. The compound of claim 16 wherein

5 R₁₅ is selected from the group consisting of hydroxy and



wherein R₁₂ is O or S;

or a pharmaceutically acceptable salt or tautomer thereof.

10 18. The compound of claim 17 wherein R₁₁ is C₅-C₉ alkyl;

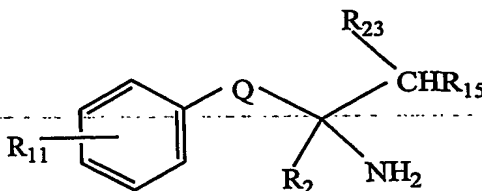
R₁₅ is OH and

R₃ is selected from the group consisting of CH₃, CH₂CH₃, CH₂OH,
CH₂CH₂OH and CH₂CH₂CH₂OH.

15 19. A composition comprising a compound of claim 1, 2, 6, 8, 11 or 16
and

a pharmaceutically acceptable carrier.

20. A composition comprising a compound represented by the formula



20

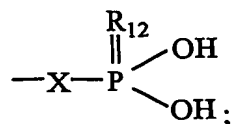
wherein R₁₁ is C₅-C₁₈ alkyl or C₅-C₁₈ alkenyl;

Q is selected from the group consisting of C₃-C₆ optionally substituted
cycloalkyl, C₃-C₆ optionally substituted heterocyclic, C₃-C₆ optionally substituted
aryl, C₃-C₆ optionally substituted heteroaryl and -NH(CO)-;

25 R₂ is selected from the group consisting of H, C₁-C₄ alkyl and (C₁-C₄
alkyl)OH;

R₂₃ is H or C₁-C₄ alkyl, and

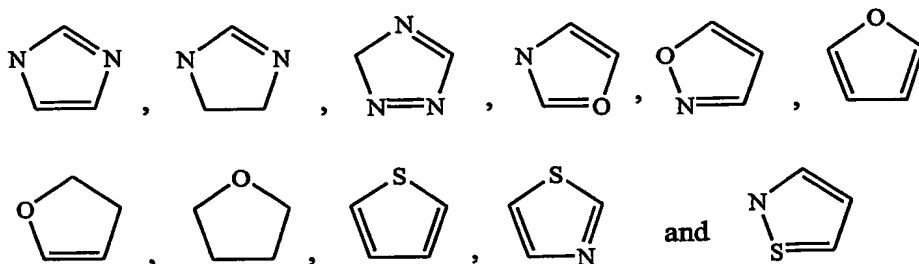
R₁₅ is selected from the group consisting of hydroxy, phosphonate, and



wherein X and R₁₂ is selected from the group consisting of O and S;
or a pharmaceutically acceptable salt or tautomer thereof and

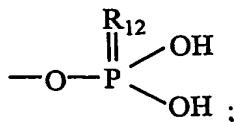
5 a pharmaceutically acceptable carrier.

21. The composition of claim 20 wherein Q is selected from the group consisting of



10

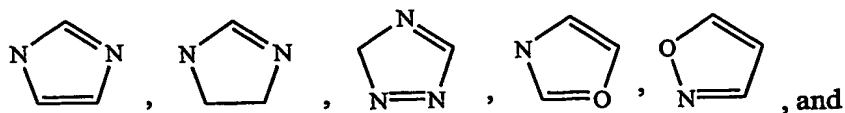
22. The composition of claim 21 wherein R₁₅ is selected from the group consisting of hydroxy and



wherein R₁₂ is O or S.

15

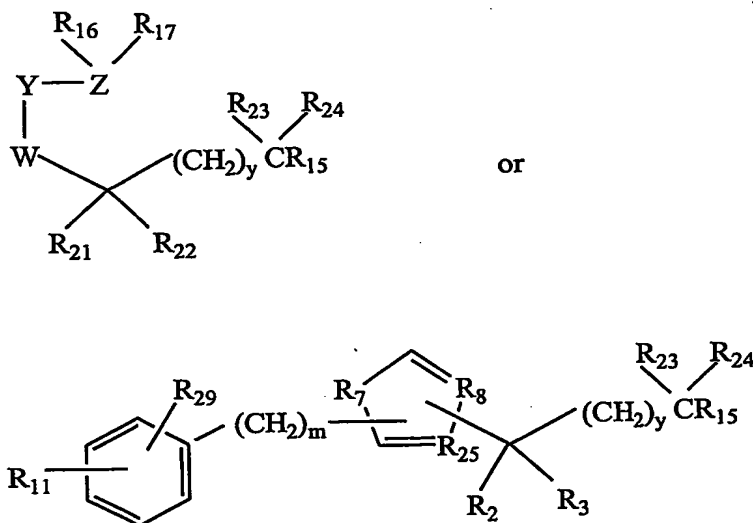
23. The composition of claim 22 wherein Q is selected from the group consisting of



R₁₅ is OH;

20 or a pharmaceutically acceptable salt or tautomer thereof.

24. A method for modulating the activity of an S1P receptor, said method comprising the step of contacting said receptor with a compound represented by the formula:



5

wherein

W is $\text{CR}_{27}\text{R}_{28}$ or $(\text{CH}_2)_n\text{NH}(\text{CO})$;

wherein R_{27} and R_{28} are independently selected from the group consisting of H, halo and hydroxy;

Y is selected from the group consisting of a bond, CR_9R_{10} , carbonyl, NH, O or

10 S;

wherein R_9 and R_{10} are independently selected from the group consisting of H, halo, hydroxy and amino;

Z is CH_2 , aryl, halo substituted aryl or heteroaryl;

R_{11} and R_{16} are independently selected from the group consisting of $\text{C}_1\text{-C}_{12}$

15 alkyl, $\text{C}_2\text{-C}_{12}$ alkenyl, $\text{C}_2\text{-C}_{12}$ alkynyl, $\text{C}_5\text{-C}_{12}$ alkoxy, $(\text{CH}_2)_p\text{O}(\text{CH}_2)_q$, $\text{C}_5\text{-C}_{10}$ (aryl) R_{20} , $\text{C}_5\text{-C}_{10}$ (heteroaryl) R_{20} , $\text{C}_5\text{-C}_{10}$ (cycloalkyl) R_{20} , $\text{C}_5\text{-C}_{10}$ alkoxy(aryl) R_{20} , $\text{C}_5\text{-C}_{10}$ alkoxy(heteroaryl) R_{20} and $\text{C}_5\text{-C}_{10}$ alkoxy(cycloalkyl) R_{20} ;

wherein R_{20} is H or $\text{C}_1\text{-C}_{10}$ alkyl;

R_{29} is H or halo;

20 R_{17} is selected from the group consisting of H, halo, NH_2 , $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, $\text{C}_1\text{-C}_6$ alkylamino, $\text{C}_1\text{-C}_6$ alkylcyano and $\text{C}_1\text{-C}_6$ alkylthio;

R_2 , and R_{21} are both NH_2 ;

R_3 is selected from the group consisting of H, C₁-C₆ alkyl, (C₁-C₄ alkyl)OH, and (C₁-C₄ alkyl)NH₂;

R_{22} is selected from the group consisting of C₁-C₆ alkyl, (C₁-C₄ alkyl)OH and (C₁-C₄ alkyl)NH₂;

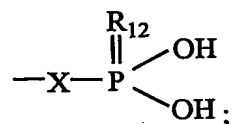
5 R_{23} is selected from the group consisting of H, F, CO₂H, OH, C₁-C₆ alkyl, (C₁-C₄ alkyl)OH, and (C₁-C₄ alkyl)NH₂;

R_{24} is selected from the group consisting of H, F and PO₃H₂, or R_{23} together with R_{24} and the carbon to which they are attached form a carbonyl group;

10 R_{25} , R_7 and R_8 are independently selected from the group consisting of O, S, CHR₂₆, CHR₂₆, NR₂₆, and N;

wherein R_{26} is H, F or C₁-C₄ alkyl;

R_{15} is selected from the group consisting of hydroxy, phosphonate, and



wherein R_{12} is selected from the group consisting of O, NH and S;

15 X is selected from the group consisting of O, NH and S;

y and m are integers independently ranging from 0 to 4;

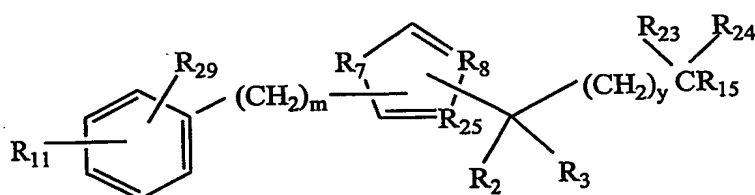
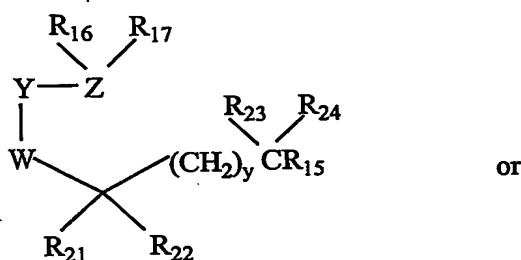
p and q are integers independently ranging from 1 to 10;

n is an integer ranging from 0 to 10;

or a pharmaceutically acceptable salt or tautomer thereof, with the proviso that W and

20 Y are not both methylene.

25. A method of providing immuno-modulation to a patient in need thereof, said method comprising the step of administering to said patient a composition comprising a compound represented by the formula:



wherein

W is $\text{CR}_{27}\text{R}_{28}$ or $(\text{CH}_2)_n\text{NH}(\text{CO})$;

wherein R_{27} and R_{28} are independently selected from the group

5 consisting of H, halo and hydroxy;

Y is selected from the group consisting of a bond, CR_9R_{10} , carbonyl, NH, O or

S;

wherein R_9 and R_{10} are independently selected from the group

consisting of H, halo, hydroxy and amino;

10 Z is CH_2 , aryl, halo substituted aryl or heteroaryl;

R_{11} and R_{16} are independently selected from the group consisting of $\text{C}_1\text{-C}_{18}$ alkyl, $\text{C}_2\text{-C}_{18}$ alkenyl, $\text{C}_2\text{-C}_{18}$ alkynyl, $\text{C}_5\text{-C}_{18}$ alkoxy, $(\text{CH}_2)_p\text{O}(\text{CH}_2)_q$, $\text{C}_5\text{-C}_{10}$ (aryl) R_{20} , $\text{C}_5\text{-C}_{10}$ (heteroaryl) R_{20} , $\text{C}_5\text{-C}_{10}$ (cycloalkyl) R_{20} , $\text{C}_5\text{-C}_{10}$ alkoxy(aryl) R_{20} , $\text{C}_5\text{-C}_{10}$ alkoxy(heteroaryl) R_{20} and $\text{C}_5\text{-C}_{10}$ alkoxy(cycloalkyl) R_{20} ;

15 wherein R_{20} is H or $\text{C}_1\text{-C}_{10}$ alkyl;

R_{29} is H or halo;

R_{17} is selected from the group consisting of H, halo, NH_2 , $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, $\text{C}_1\text{-C}_6$ alkylamino, $\text{C}_1\text{-C}_6$ alkylcyano and $\text{C}_1\text{-C}_6$ alkylthio;

R_2 , and R_{21} are both NH_2 ;

20 R_3 is selected from the group consisting of H, $\text{C}_1\text{-C}_6$ alkyl, $(\text{C}_1\text{-C}_4 \text{ alkyl})\text{OH}$, and $(\text{C}_1\text{-C}_4 \text{ alkyl})\text{NH}_2$;

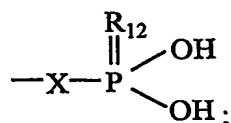
R₂₂ is selected from the group consisting of C₁-C₆ alkyl, (C₁-C₄ alkyl)OH and (C₁-C₄ alkyl)NH₂;

R₂₄ is selected from the group consisting of H, F and PO₃H₂, or R₂₃ together with R₂₄ and the carbon to which they are attached form a carbonyl group;

5 R₂₅, R₇ and R₈ are independently selected from the group consisting of O, S, CHR₂₆, CHR₂₆, NR₂₆, and N;

wherein R₂₆ is H, F or C₁-C₄ alkyl;

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and



10

wherein R₁₂ is selected from the group consisting of O, NH and S;

X is selected from the group consisting of O, NH and S;

y and m are integers independently ranging from 0 to 4;

p and q are integers independently ranging from 1 to 10;

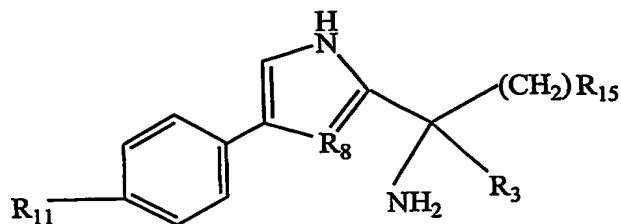
n is an integer ranging from 0 to 10;

15 or a pharmaceutically acceptable salt or tautomer thereof, with the proviso that W and Y are not both methylene.

26. The method of claim 25 further comprising the step of administering a second immuno-modulatory agent selected from the group consisting of cyclosporine, tacrolimus, rapamycin, azathioprine, and corticosteroids such as prednisolone and prednisone.

20

27. The method of claim 25 wherein the compound has the general formula:



25

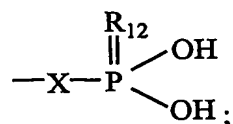
wherein R_{11} is selected from the group consisting of C_1 - C_{22} alkyl, C_2 - C_{22} alkenyl and C_2 - C_{22} alkynyl;

R_3 is selected from the group consisting of NH_2 , OH, C_1 - C_6 alkyl, $(C_1$ - C_4 alkyl)OH, $-(C_1$ - C_4 alkyl) NH_2 , $(C_1$ - C_4 alkyl)aryl(C_0 - C_4 alkyl) and $(C_1$ - C_4

5 alkyl)aryloxyaryl(C_0 - C_4 alkyl);

R_8 is selected from the group consisting of O, S and N.

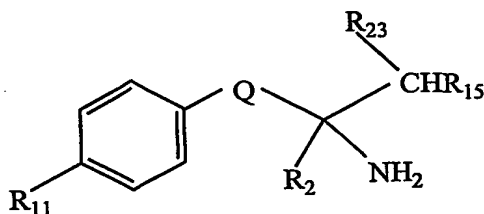
R_{15} is selected from the group consisting of hydroxy, phosphonate, and



wherein R_{12} is selected from the group consisting of O, NH and S; and

10 X is selected from the group consisting of O, NH and S; or a pharmaceutically acceptable salt or tautomer thereof.

28. A method of promoting wound healing in a warm blooded vertebrate, said method comprising the step of administering a composition comprising a a
15 compound of the general structure:



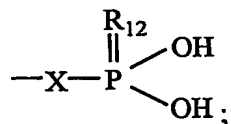
wherein R_{11} is C_5 - C_{18} alkyl or C_5 - C_{18} alkenyl;

Q is selected from the group consisting of C_3 - C_6 optionally substituted
cycloalkyl, C_3 - C_6 optionally substituted heterocyclic, C_3 - C_6 optionally substituted
20 aryl, C_3 - C_6 optionally substituted heteroaryl and $-NH(CO)-$;

R_2 is selected from the group consisting of H, C_1 - C_4 alkyl and $(C_1$ - C_4 alkyl)OH;

R_{23} is H or C_1 - C_4 alkyl, and

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

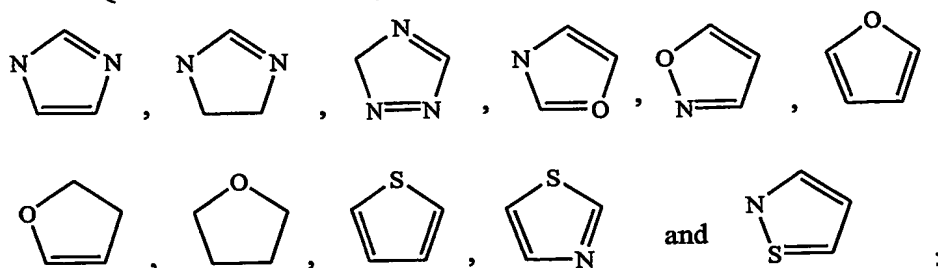


wherein X and R₁₂ is selected from the group consisting of O and S;
or a pharmaceutically acceptable salt or tautomer thereof.

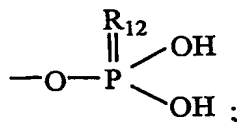
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29. The method of claim 28 wherein

Q is selected from the group consisting of -NH(CO)-,



and R₁₅ is selected from the group consisting of hydroxy and

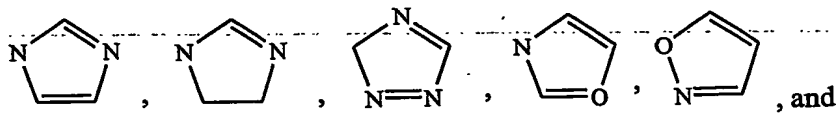


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wherein R_{12} is O or S.

30. . The method of claim 29 wherein

Q is selected from the group consisting of

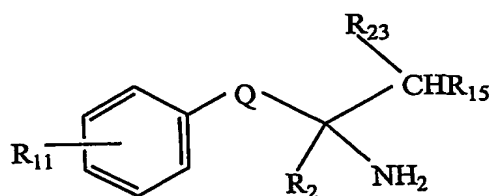


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R₁₅ is OH;

or a pharmaceutically acceptable salt or tautomer thereof.

31. A method for treating a patient suffering from a disease associated
20 with abnormal cell growth, said method comprising the steps of administering a a
compound of the general structure:



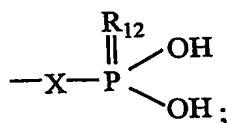
wherein R_{11} is located in the meta or para position and is selected from the group consisting of C_5 - C_{18} alkyl and C_5 - C_{18} alkenyl;

Q is selected from the group consisting of C_3 - C_6 optionally substituted cycloalkyl, C_3 - C_6 optionally substituted heterocyclic, C_3 - C_6 optionally substituted aryl C_3 - C_6 optionally substituted heteroaryl and $-NH(CO)-$;

R_2 is selected from the group consisting of H, C_1 - C_4 alkyl and $(C_1$ - C_4 alkyl)OH;

R_{23} is H or C_1 - C_4 alkyl, and

R_{15} is selected from the group consisting of hydroxy, phosphonate, and

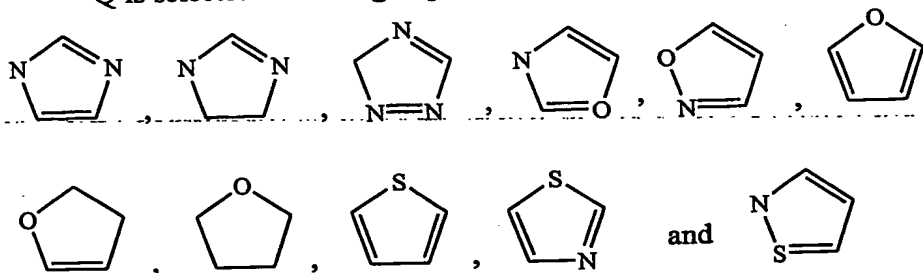


wherein X and R_{12} is selected from the group consisting of O and S; or a pharmaceutically acceptable salt or tautomer thereof.

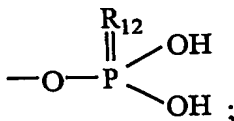
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32. The method of claim 31 wherein

Q is selected from the group consisting of $-NH(CO)-$;



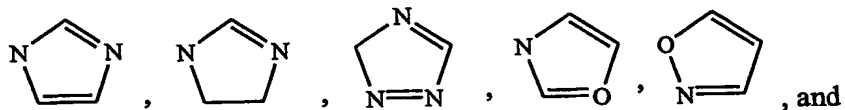
and R_{15} is selected from the group consisting of hydroxy and



20

wherein R_{12} is O or S.

33. The method of claim 32 wherein
Q is selected from the group consisting of



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R₁₅ is OH;

or a pharmaceutically acceptable salt or tautomer thereof.